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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/674,787

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Hide nobu Yaku

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EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT

PAPER NUMBER

1637

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

04/02/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/674,787

Applicant(s)

YAKU ET AL.

Examiner

Suryaprabha Chunduru

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12, 19-27 and 31-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12, 19-27 and 31-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 December 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' response to the office action filed on January 19, 2007 has been considered and acknowledged.

Status of the Application

2. Currently claims 1-12, 19-27, 31-33 are pending. Claims 13-18 and 28-30 are cancelled. All arguments and amendment have been fully considered and thoroughly reviewed and deemed persuasive in part for the reasons that follow. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. The action is made FINAL.

Response to arguments:

3. With regard to the rejection of claims 1-12, 19-27, 31-33 under 35 USC 103(a) as being obvious over Orlefors et al. in view of Maeshima et al., Applicants' arguments are fully considered and found unpersuasive. Applicants argue Orlefors teach the disadvantage of using the dATP as a substrate for luciferase reaction, and argue that Orlefors does not teach H^+ pyrophosphatase which hydrolyse pyrophosphate released during extension reaction and measuring H^+ concentration and Maeshima does not remedy the deficiency of the Orlefors' method. Applicants further argue that Maeshima et al. does not teach said deficiency and does not disclose the possible reaction of H^+ PPase with dNTPs, which are substrates for DNA extension reaction and which contain PPi within their molecular structures and thus are highly likely to react with H^+ PPase. Applicants' arguments are fully considered and found unpersuasive. First, the instant independent claims do not recite dATP as a substrate for luciferase reaction. Second, the step (b) of the independent claims 1-2, 19 recite producing pyrophosphatase when extension reaction is caused, which clearly indicates that the PPi is

released into the sample solution and the released PPi is hydrolysed by H^+ PPase. Thus the arguments based on the reaction of H^+ PPase with PPi bound to the molecular structures of dNTPs are irrelevant to the currently presented claims. Thus the limitation upon which the instant arguments depend, are not found in the instant claims. As noted in the MPEP 2145 Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants further argue that Examiner has not explained the relevance of the paragraph at page 39, coll.1, section 2.2 of Maeshima et al. with the measuring of the activity of H^+ PPase based on PPi hydrolysis. Applicants further argue that the examiner concludes that it is obvious to modify the method of Orlefors et al. with Maeshima for the purpose of developing a sensitive method and assert that the instant specification does not state that an object of the present invention is to develop 'sensitive' method. Applicants' arguments are found unpersuasive. As noted in MPEP 2144 the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. >See, e.g., *In re Kahn*, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006) and there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention. Further Applicants assert that Maeshima et al. does not teach vascular membrane associate H^+ PPase can be used to measure the release of PPi in a DNA extension reaction. Applicants also argue that the Examiner cited pages of Orlefors does not teach measuring a primer extension product. Applicants' arguments are fully considered and

found unpersuasive. With reference to attacking references individually, Examiner notes that According to MPEP 2145 One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is noted that the cited paragraph of Maeshima et al. is self explanatory and it does teach measuring the activity of H^+ PPase because the free energy change for PPi hydrolysis is calculated based on the H^+ /PPi stoichiometry of H^+ PPase and kinetics of the enzyme activity. Thus the cited paragraph does indicate measuring the H^+ PPase activity based on PPi hydrolysis and it is relevant to the instant claims because the instant claims depend said limitation. Further the cited pages of Orlefors clearly teach continuous monitoring of PPi release during primer extension using luciferin–luciferase reaction. Even though Orlefors teach measuring PPi release in a Luciferase reaction system, Orlefors does not teach the use of a membrane bound H^+ PPase to monitor or measure the PPi release as a by product in primer extension. Maeshima clearly teach measuring PPi using membrane bound H^+ PPase and also teach that that the PPi is a byproduct of the reaction involving DNA polymerization reactions, in growing tissues, which is self explanatory that the DNA synthesis occur in growing tissue and the primer extension reactions take place and PPi is released as a by product.

With regard to the arguments based on no teaching or suggest ether in combination or referecnes alone, examiner notes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5

USPQ2d 1596 (Fed. Cir. 1988) and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.1992).

In this case, specific motivation is provided in the rejection, which states that an ordinary person skill in the art would have been motivated to combine the method taught by the Orlefors et al. with the inclusion of vacuolar membrane associated H^+ pyrophosphatase to measure the release of PPi to achieve expected advantage of developing a sensitive method for detecting base sequence of a target nucleic acid. The ordinary artisan would have a reasonable expectation of success that the inclusion of said vacuolar membrane associated H^+ pyrophosphatase would result in a sensitive measurement of PPi released during extension reaction by measuring H^+ concentration on at least either one side of the membrane because Maeshima explicitly taught that the by-product produced by polymerization of DNA or RNA is scavenged by vacuolar H^+ - PPase, and uses it as a source of energy for transporting protons into the vacuoles (see page 38, col. 1, line 21-27, page 45, col. 1, paragraph 1, Fig. 4) and such modification of the method would be obvious over the cited prior art. Accordingly the rejection is maintained herein.

4. With regard to the rejection of claims 1-12, 19-27, 31-33 under provisional double patenting, Applicants' arguments and submission of a terminal disclaimer have been fully considered and the rejection is withdrawn herein in view of the terminal disclaimer.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Suryaprabha Chunduru
SURYAPRABHA CHUNDURU 3/28/07
PRIMARY EXAMINER